

Rifapentine and Isoniazid 12 week regimen

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August 1, 2013

Some Basics

- LTBI vs Active TB
 - The importance of designating active vs latent disease
 - A person with latent TB infection
 - Usually has a skin test or blood test result indicating TB infection
 - Has a normal chest x-ray and a negative sputum test
 - Has TB bacteria in his/her body that are alive, but inactive
 - Does not feel sick
 - Cannot spread TB bacteria to others
 - Needs treatment for latent TB infection to prevent TB disease; however, if exposed and infected by a person with multidrug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option

Treatment of Latent TB

- Regimen choices
 - INH alone (daily vs twice weekly)
 - 9 months
 - 6 months
 - Rifampin alone
 - 4 months
 - Rifapentine and INH
 - 12 weeks of DOT therapy

Individual meds

- Rifapentine
 - Mechanism of Action: Inhibits DNA dependent RNA polymerase – Rifamycin
 - Metabolism: Liver CYP450, 3A4 inducer
 - Many drug interactions
 - Serious side effects: blood dyscrasias, hepatotoxicity, interstitial nephritis, pancreatitis

- Isoniazid

- Mechanism of Action: inhibits lipid and nucleic acid synthesis. (bactericidal)
- Metabolism: Liver; CYP450: 2C19(mod), 3A4(mild) inhibitor; 2E1 (strong inducer)
- Many drug interactions
- Dyscrasias, hepatotoxicity, optic neuritis, toxic psychosis, seizures, neuropathies.

List of eligiblities for this therapy

- recent exposure to contagious TB
- conversion from negative to positive tuberculin skin test (TST) or Interferon Gamma Release Assay (IGRA) within previous 2 years
- radiographic findings of inactive, “healed” pulmonary TB
- HIV/AIDS but not taking antiretroviral medications
- medical or social circumstances that make adherence and completion of longer regimens unlikely

List of ineligibilities

- Children younger than 2 years of age
- Patients with HIV/AIDS who are taking antiretroviral treatment
- Patients with presumed INH or rifampin-resistant LTBI
- Pregnant women or women expecting to become pregnant during treatment

DOT is mandatory.

Studies supporting the efficacy and tolerability of INH-RPT were based on treatment protocols using DOT provided by public health agencies.

Experiences with therapy in patient care

- Adverse events
 - Hypotension
 - Nausea/vomiting
 - Neuropathy
 - Hepatotoxicity
 - Hypersensitivity reaction
 - This is the most concerning

Hypersensitivity Reaction

- Hypersensitivity reactions may include a flu like syndrome (e.g. fever, chills, headaches, dizziness, musculoskeletal pain), thrombocytopenia, shortness of breath or other signs and symptoms including wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema, hypotension or shock.
- If moderate to severe reaction (e.g. thrombocytopenia, hypotension), hospitalization or life-threatening event
Discontinue treatment
- If mild reaction (e.g. rash, dizziness, fever)
 - *Continue to monitor patient closely with a low threshold for discontinuing treatment*

Hydration Protocol

- By the implementation of a hydration protocol prior to initiation of dual therapy we have been able to reduce the number of reactions we have had.
- Attached.

West Virginia Department of Health and Human Resources - Division of TB Elimination

**PROTOCOL FOR HYDRATION WHEN USING RIFAPINTINE AND ISONIZID
TWELVE WEEK DRUG REGIMEN**

DATE: September 1, 2012

TO: All WV Local Health Departments

FROM: Dominic Gaziano, MD
Medical Director, WV Division of TB Elimination

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1. One hour before dosing with RPT/INH have patient eat a small nonfat meal.
 2. One hour before dosing with RPT/INH have patient drink 8 ozs. of no caffeine fluid.
 3. Have patient continue to drink 8 ozs. of no caffeine fluid every hour for six hours after dosing.
 4. Provide education to the patient regarding importance of this hydration protocol to prevent side effects of the medication which can include severe hypotension.

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**Protocol For Hydration When Using Rifapentine And Isonizid
Twelve Week Drug Regimen**

1. One hour before taking medications eat a small nonfat meal.
2. One hour before taking medications drink 8 ozs of non caffeine fluid.
3. Continue to drink 8 ozs of non caffeine fluid every hour for six hours after taking medicine.
4. This hydration protocol is to prevent side effects of the medication which can include severe low blood pressure.

Protocol per WV Division of TB Elimination
Medical Director Dominic Gaziano, MD